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TO	Examiner Lauren Q. Wells	FAX	(703) 746-5231
PHONE	(703) 305-1878	PAGES	6 (INCLUDING THIS SHEET)
FROM	Sonia K. Guterman, Ph.D.	DATE	10/09/01
RE	Appln. No.: 09/521,264 Applicant: Groman et al. Grp./Art Unit: 1619		
OUR FILE	1275/190	YOUR FILE	

## COMMENTS

Dear Examiner Wells:

With this fax cover sheet we are sending supporting material to be attached to our Response A of October 4, 2001, in response to your Office Action of July 5, 2001.

We would appreciate it if you would please attach this material to the Response when you receive it. The material is relevant to our arguments on use of the word "derivative" in response to a rejection under 35 U.S.C. section 112, paragraph 2. Thank you.

Sincerely yours,



Sonia K. Guterman, Ph.D.

SKG/gam

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GROUP 1600

THE  
SYSTEMATIC  
IDENTIFICATION  
OF ORGANIC COMPOUNDS

*a laboratory manual*

6th. ed.

Ralph L. Shriner

Visiting Professor of Chemistry  
Southern Methodist University, Dallas, Texas 75275  
Formerly Professor and Head of the  
Department of Chemistry  
University of Iowa, Iowa City, Iowa

The late Reynold C. Fuson

Formerly Distinguished Visiting Professor  
University of Nevada, Reno, Nevada 89507  
Formerly Professor of Organic Chemistry and  
Member of the Center for Advanced Study  
University of Illinois, Urbana, Illinois

David Y. Curtin

Professor of Chemistry  
University of Illinois  
Urbana, Illinois 61701

Terence C. Morrill

Professor of Chemistry  
Rochester Institute of Technology  
Rochester, N.Y. 14623

JOHN WILEY & SONS

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## 2.9 THE PREPARATION OF DERIVATIVES

Refer to Chapter 6; pp. 134-355.

The list of possible compounds that results from the preceding steps in the examination of an unknown may contain a number of structural possibilities. The next step in identification is the confirmation of the identity of one of these possibilities with the unknown and the simultaneous demonstration that each of the remaining possibilities differs in some way from the unknown. This final proof can be done by the preparation of derivatives.

In eliminating compounds from the list of possibilities, one is not restricted to the use of derivatives. Any sufficiently characteristic property, such as specific gravity, refractive index, optical rotation, neutralization equivalent, or spectra may be employed.

**The Properties of a Satisfactory Derivative.** (1) A satisfactory derivative should be easily and quickly made and readily purified. This generally means that the derivative must be a solid, because, in the isolation and purification of small amounts of material, solids afford greater ease of manipulation, and melting points are more accurately and more easily determined than boiling points. The most suitable derivatives melt above 50°C but below 250°C. Most compounds that melt below 50°C are difficult to crystallize, and a melting point above 250°C is undesirable on account of possible decomposition and because the stem correction of the thermometer often amounts to several degrees.

(2) The derivative must be prepared by a reaction that occurs in good yield. Processes accompanied by rearrangements and side reactions are to be avoided.

(3) The derivative should possess properties distinctly different from those of the original compound. Generally, this means that there should be a marked difference between its melting point and that of the parent substance.

(4) The derivative chosen should be one that will single out uniquely one compound from among all the possibilities. Hence the melting points of the derivatives to be compared should differ from each other by at least 5°C.

Consult Chapter 6 and select a suitable derivative from those suggested. It will be noted that derivatives that are satisfactory for purposes of identification are numerous but often of limited scope.

In deciding whether a compound actually possesses the physical constants observed, considerable latitude must be allowed for experimental error. Thus, if the boiling point is very high or the melting point very low, the range must be extended somewhat beyond 5°C. Other constants such as specific gravity (p. 52), refractive index (p. 58), and neutralization equivalents (p. 268) may be used, with proper allowance for experimental error, to exclude compounds from the list of possibilities. A complete list of possible compounds with derivatives for each should always be made even though a product obtained in the classification tests appears to be a suitable derivative.

Examination of the list of possibilities often suggests further functional group tests to be attempted. For example, if a list of possible nitro compounds contains a

## CHAPTER SIX

### *the detection and confirmation of functional groups: complete structure determination*

As a result of earlier purity (Chapter 3), physical (Chapter 3), spectral (Chapter 4), and chemical (Chapters 3, 4, and 5) determinations, the student probably has a reasonable idea regarding the identity of the unknown compound; it is virtually certain that additional, thorough characterization is in order. A very large proportion of organic compounds lend themselves to final characterization by the chemical and spectral tests described in this chapter. As a result of the characterizations described in earlier chapters, most unknowns should be understood well enough to allow the student to choose the section (or sections) below that describe testing procedures for that particular class of compound. These tests are indexed below by functional group as well as by reagent.

Each section corresponding to a functional group (or groups) is composed of the following parts:

1. Chemical tests
2. Illustrations and descriptions of ir and nmr spectral characteristics followed by a brief statement of mass spectral characteristics
3. Derivatization procedures
4. Reference to unusual physical or chemical characterization procedures

Despite the tremendous importance and ease of spectral analyses, chemical tests are indispensable to complete characterization; thus these "wet" tests are nearly always used for compound identification. For example, the double bond of 1,2-dimethylcyclohexene is difficult to detect spectrally; chemical addition reactions (e.g., of bromine or of potassium permanganate) to such double bonds are, however, usually rapid. Thus, any student enchanted with spectral analysis to the exclusion of chemical analysis may be severely hampered in his or her attempt to identify a compound.

In earlier sections we have merely described how to determine ir and nmr spectra; detailed discussion of the theory necessary to interpret such spectra is left to other textbooks. We shall, however, describe many of the spectral absorptions (for example, nmr bands) of standard molecular classes without discussing the theory (for example, of spin-spin coupling of nmr spectrometry).

Derivatization procedures have somewhat diminished in stature with the advent of organic spectrometry. Although it certainly is no longer as important to make, for example, both a semicarbazone and a dinitrophenylhydrazone of an aldehyde, derivatization procedures still provide both physical data (for example, melting point) and an insight to the chemistry of the new substrate. Chemists should also remember that certain "derivatizations" are really "conversions" of one common organic compound into another. Conversion (e.g., oxidizing a secondary alcohol to a ketone) may yield a compound that should also be thoroughly characterized. Indeed, many derivatizations are really syntheses or "preps."

The tables of data of derivatives in various references should be consulted to see if m.p. data are available; if the m.p. is not known, the chemist may have a sample that is essentially another unknown to characterize. Tabulated physical constants such as refractive indices are useful for confirming chemical constitution. One should supplement these comparisons with references to ir, nmr, and less frequently mass spectra that should be compared to the spectra of the unknown for "fingerprint" identification.

As far as spectral analysis is concerned, we shall be concerned largely with an interpretive rather than a "fingerprint" approach. We shall be concerned with identifying spectral bands that can be used to detect organic functional groups and structural units in the molecule. We shall then combine these results with results from chemical reactions to characterize completely the sample at hand.

Finally, it is intuitively reasonable that special characterizations should be employed for certain classes of organic compounds. One expects, for example, that the specific rotation,  $[\alpha]$ , of amino acids (in view of the fact that they often have chiral centers) would be useful.

It cannot be overemphasized that the thorough organic chemist must consult additional references (see Chapter 10) to seek out additional procedures and data to characterize many compounds.

Since no textbook intended for student use can hope to include all chemical tests, tables of reference to many chemical tests described in *Organic Structure Determination*, by D. J. Pasto and C. R. Johnson (Prentice-Hall, Englewood Cliffs, N.J., 1969), and in *Semimicro Qualitative Organic Analyses*, 3rd ed., by N. D. Cheronis, J. B. Entrikin, and E. M. Hodnett (Wiley-Interscience, New York,